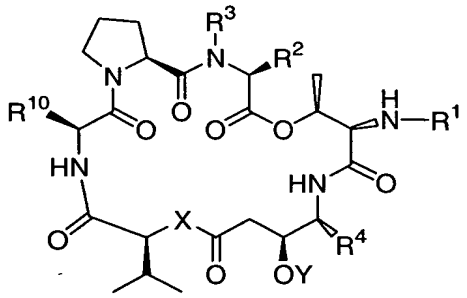
Amendments to the Claims

Please add new claims 56-61.

The listing of claims will replace all prior versions and listings of claims in the application.

1. (Currently Amended) A composition comprising a tamandarin analog having the structure



wherein:

i) R^1 is selected from the group consisting of

-(N-methyl)leucine-deoxo-proline,

-(N-methyl)leucine-deoxo-proline-lactate,

-(N-methyl)leucine-deoxo-proline-pyruvate,

-(N-methyl)leucine-deoxo-proline-lactate-(a first fluorophore),

-(N-methyl)leucine-deoxo-proline-lactate-glutamine-pyroglutamate,

-(N-methyl)leucine-deoxo-proline-lactate-glutamine-cyclopentanoate,

-(N-methyl)leucine-deoxo-proline-alanine-leucine-pyroglutamate

-(N-methyl)leucine-deoxo-proline-(N-methyl-alanine)-leucine-pyroglutamate,

-(N-methyl)leucine-dehydro-proline,

-(N-methyl)leucine-dehydro-proline-lactate,

-(N-methyl)leucine-dehydro-proline-pyruvate,

-(N-methyl)leucine-dehydro-proline-lactate-(a first fluorophore),

-(N-methyl)leucine-dehydro-proline-lactate-glutamine-pyroglutamate,

-(N-methyl)leucine-dehydro-proline-lactate-glutamine-cyclopentanoate,

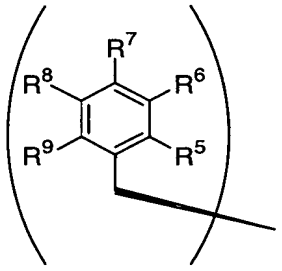
-(N-methyl)leucine-dehydro-proline-alanine-leucine-pyroglutamate, and

-(N-methyl)leucine-dehydro-proline-(N-methyl-alanine)-leucine-pyroglutamate;

ii) ~~either~~ R^2 and R^3 are one of

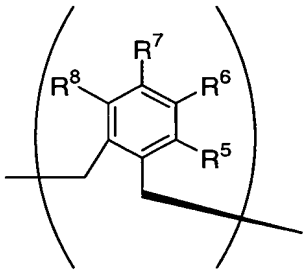
(a) R^3 is selected from the group consisting of $-CH_3$ and -H;

and R^2 is selected from the group consisting of an isoleucine side chain, a valine side chain, an alanine side chain, a norleucine side chain, a norvaline side chain, a leucine side chain, a histidine side chain, a tryptophan side chain, an arginine side chain, a lysine side chain, a second fluorophore, and a substituent having the structure



; ~~or~~ and

(b) R^2 and R^3 together are a substituent having the structure



iii) each of R^5, R^6, R^7, R^8, and R^9, when present, is independently selected from the group consisting of -H, -OH, $-OCH_3$, $-CO(C_6H_5)$, -Br, -I, -F, -Cl, $-CH_3$, and $-C_2H_5$;

iv) R^4 is selected from the group consisting of an isoleucine side chain and a valine side chain;

v) X is selected from the group consisting of -O- and ~~-(NH)-~~ -NH-;

vi) Y is selected from the group consisting of -H and a hydroxyl protecting group;

vii) R^{10} is selected from the group consisting of a leucine side chain and a lysine side chain; and

viii) the molecule is not tamandarin A.

2. (Original) The composition of claim 1, wherein R^1 is selected from the group consisting of

-(N-methyl)leucine-deoxo-(S)proline,

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate,

-(N-methyl)leucine-deoxo-(S)proline-pyruvate,

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-(a first fluorophore),

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-glutamine-pyroglutamate,

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-glutamine-cyclopentanoate,

-(N-methyl)leucine-deoxo-(S)proline-alanine-leucine-pyroglutamate,

-(N-methyl)leucine-deoxo-(S)proline-(N-methyl-alanine)-leucine-pyroglutamate,

-(N-methyl)leucine-dehydro-(S)proline,

-(N-methyl)leucine-dehydro-(S)proline-(S)lactate,

-(N-methyl)leucine-dehydro-(S)proline-pyruvate,

-(N-methyl)leucine-dehydro-(S)proline-(S)lactate-(a first fluorophore),

-(N-methyl)leucine-dehydro-(S)proline-(S)lactate-glutamine-pyroglutamate,

-(N-methyl)leucine-dehydro-(S)proline-(S)lactate-glutamine-cyclopentanoate,

-(N-methyl)leucine-dehydro-(S)proline-alanine-leucine-pyroglutamate and

-(N-methyl)leucine-dehydro-(S)proline-(N-methyl-alanine)-leucine-pyroglutamate.

3. (Currently Amended) The composition of claim 1, wherein R^1 is selected from the group consisting of

~~-(N-methyl)leucine-deoxo-(S)proline,~~

~~-(N-methyl)leucine-deoxo-(S)proline-(S)lactate,~~

~~-(N-methyl)leucine-deoxo-(S)proline-pyruvate,~~

~~-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-(a first fluorophore),~~

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-(S)glutamine-(S)pyroglutamate,

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-(S)glutamine-(S)cyclopentanoate,

-(N-methyl)leucine-deoxo-(S)proline-(S)alanine-(S)leucine-(S)pyroglutamate, and

-(N-methyl)leucine-deoxo-(S)proline-(N-methyl-S-alanine)-(S)leucine-(S)pyroglutamate,

~~-(N-methyl)leucine-dehydro-(S)proline,~~

~~-(N-methyl)leucine-dehydro-(S)proline-(S)lactate,~~

-(N-methyl)leucine-deoxo-(S)proline-pyruvate,

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-(a first fluorophore),

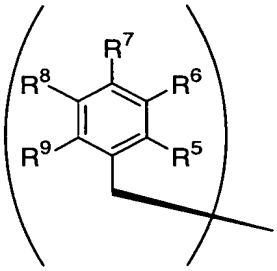
-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-(S)glutamine-(S)pyroglutamate,

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-(S)glutamine-(S)cyclopentanoate,

-(N-methyl)leucine-deoxo-(S)proline-(S)alanine-(S)leucine-(S)pyroglutamate, and

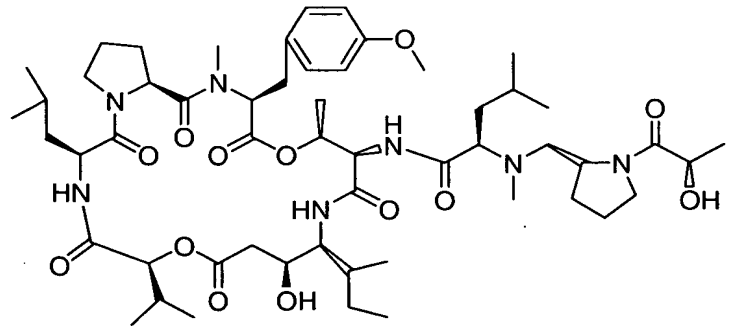
-(N-methyl)leucine-deoxo-(S)proline-(N-methyl-S-alanine)-(S)leucine-(S)pyroglutamate.

4. (Currently Amended) The composition of claim 1, wherein R^2 is

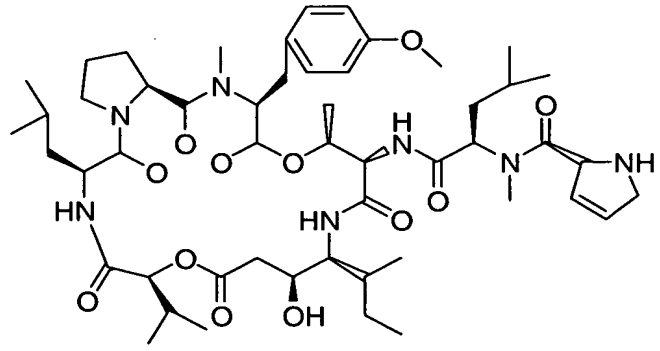


R^3 is methyl, R^4 is an isoleucine side chain, each of R^5, R^6, R^8, and R^9 is ~~a hydride radical~~ -H, R^7 is methoxy, R^{10} is a leucine side chain, X is -O-, and Y is ~~a hydride radical~~ -H.

5. (Currently Amended) The composition of claim 1, wherein the tamandarin analog is compound 201 having the structure

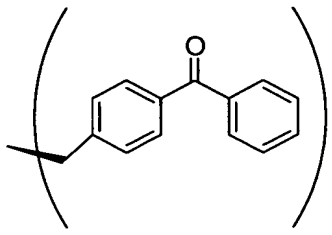


6. (Currently Amended) The composition of claim 1, wherein the tamandarin analog is compound 203 having the structure



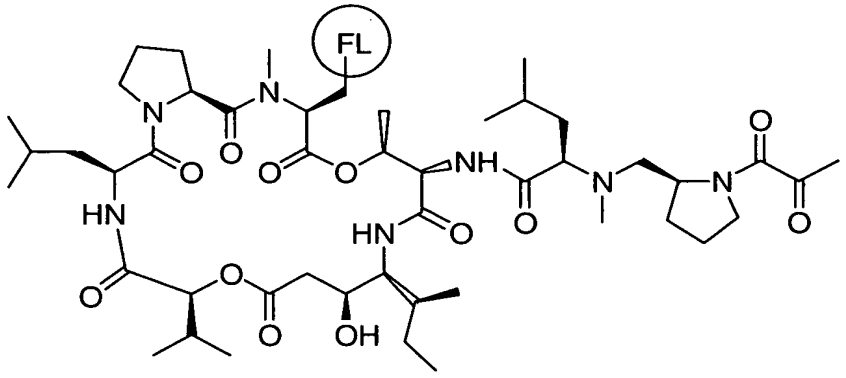
7. (Original) The composition of claim 1, wherein R^1 is -(N-methyl)leucine-deoxo-(S)proline-lactate.

8. (Original) The composition of claim 1, wherein Y is -H, and wherein R^2 has the structure



9. (Original) The composition of claim 1, wherein R^2 is a lysine side chain and Y is -H.

10. (Original) The composition of claim 1, wherein the didemnin analog has the following structure, wherein FL is a fluorophore



11. (Currently Amended) The composition of claim 1, wherein X is ~~-(NH)-~~ -NH-.

12. (Original) The composition of claim 1, further comprising a pharmaceutically acceptable carrier.

13. (Original) A support having the tamandarin analog of claim 1 covalently attached thereto.

14. (Original) A method of inhibiting protein synthesis in a cell, the method comprising administering the composition of claim 1 to the cell.

15. (Original) A method of inhibiting growth of a cell, the method comprising administering the composition of claim 1 to the cell.

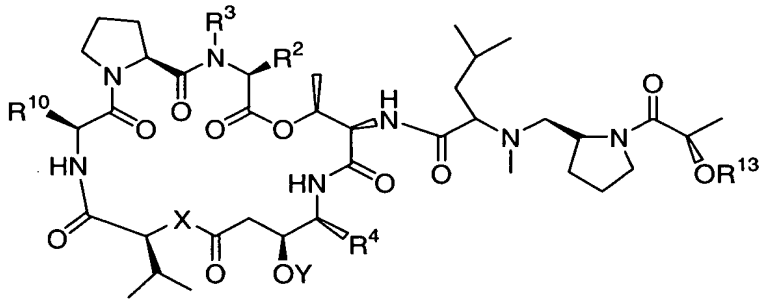
16. (Original) A method of inhibiting proliferation of a cell, the method comprising administering the composition of claim 1 to the cell.

17. (Original) A method of inhibiting tumorigenesis in a cell, the method comprising administering the composition of claim 1 to the cell.

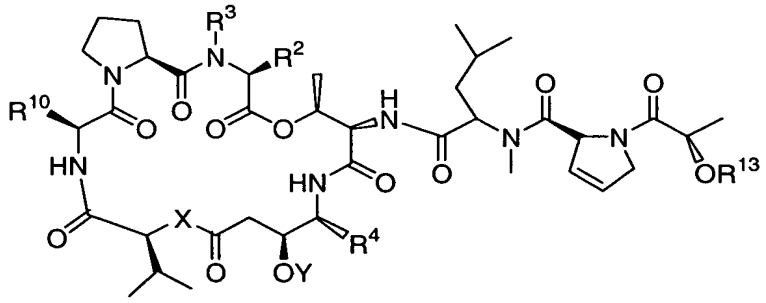
18. (Original) A method of enhancing apoptosis of a cell, the method comprising administering the composition of claim 1 to the cell.

19. (Currently Amended) A composition comprising a compound having a structure selected from the group consisting of

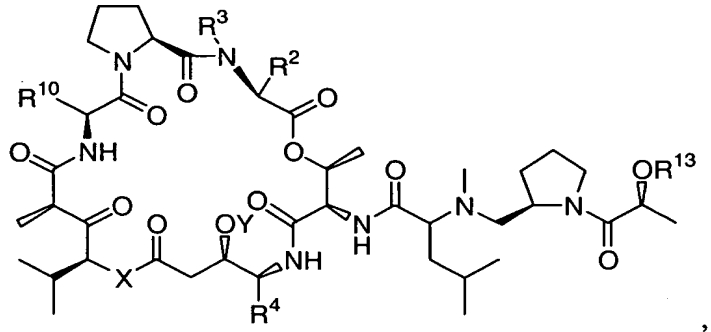
(a)



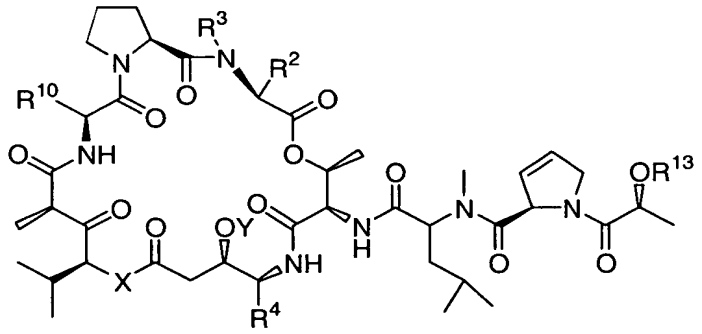
(b)



(c)



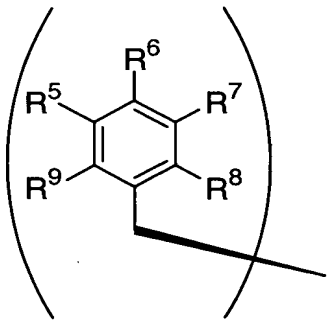
, and

(d) 

wherein:

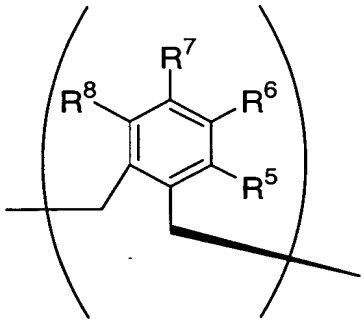
i) ~~either~~ R^2 and R^3 are one of

(a) R^3 is selected from the group consisting of $-CH_3$ and -H; and R^2 is selected from the group consisting of an isoleucine side chain, a valine side chain, an alanine side chain, a norleucine side chain, a norvaline side chain, a proline side chain, a leucine side chain, a histidine side chain, a tryptophan side chain, an arginine side chain, a lysine side chain, a second fluorophore, and a substituent having the structure



; ~~or~~ and

(b) R^2 and R^3 together are a substituent having the structure



;

ii) each of R^5, R^6, R^7, R^8, and R^9, when present, is independently selected from the group consisting of -H, -OH, $-OCH_3$, $-CO(C_6H_5)$, -Br, -I, -F, -Cl, $-CH_3$, and $-C_2H_5$;

iii) R^4 is selected from the group consisting of an isoleucine side chain and a valine side chain;

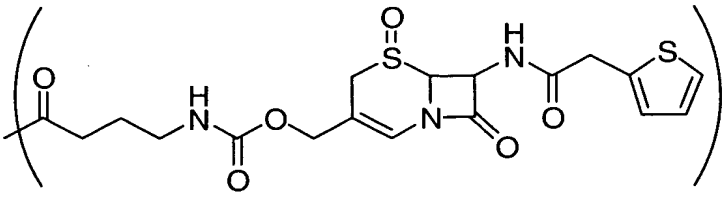
iv) X is selected from the group consisting of -O- and ~~-(NH)-~~ -NH-;

v) Y is selected from the group consisting of -H and a hydroxyl protecting group;

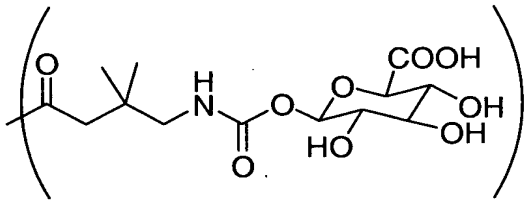
vi) R^{10} is selected from the group consisting of a leucine side chain and a lysine side chain; and

vii) R^{13} is an enzyme-cleavable moiety that is cleavable by an enzyme selected from the group consisting of a carboxypeptidase, a beta-lactamase, a beta galactosidase, a penicillin V-amidase, a cytosine deaminase, a nitroreductase, ~~a~~ an alkaline phosphatase, a beta-glucuronidase, and a catalytic antibody.

20. (Original) The composition of claim 19, wherein R^{13} has the structure



21. (Original) The composition of claim 19, wherein R^{13} has the structure



22. (Original) A method of inhibiting protein synthesis in a cell, the method comprising administering the composition of claim 19 to the cell.

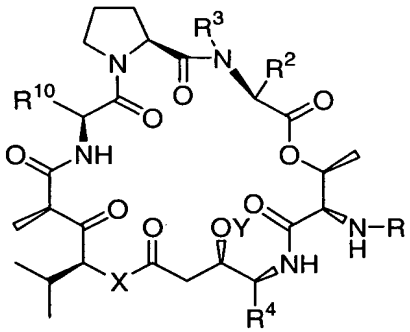
23. (Original) A method of inhibiting growth of a cell, the method comprising administering the composition of claim 19 to the cell.

24. (Original) A method of inhibiting proliferation of a cell, the method comprising administering the composition of claim 19 to the cell.

25. (Original) A method of inhibiting tumorigenesis in a cell, the method comprising administering the composition of claim 19 to the cell.

26. (Original) A method of enhancing apoptosis of a cell, the method comprising administering the composition of claim 19 to the cell.

27. (Currently Amended) A composition comprising a didemnin analog having the structure



wherein:

i) R^1 is selected from the group consisting of

-(N-methyl)leucine-deoxo-proline,

-(N-methyl)leucine-deoxo-proline-lactate,

-(N-methyl)leucine-deoxo-proline-pyruvate,

-(N-methyl)leucine-deoxo-proline-lactate-(a first fluorophore),

-(N-methyl)leucine-deoxo-proline-lactate-glutamine-pyroglutamate,

-(N-methyl)leucine-deoxo-proline-lactate-glutamine-cyclopentanoate,

-(N-methyl)leucine-deoxo-proline-alanine-leucine-pyroglutamate,

-(N-methyl)leucine-deoxo-proline-(N-methyl-alanine)-leucine-pyroglutamate,

-(N-methyl)leucine-dehydro-proline,

-(N-methyl)leucine-dehydro-proline-lactate,

-(N -methyl)leucine-dehydro-proline-pyruvate,

-(N-methyl)leucine-dehydro-proline-lactate-(a first fluorophore),

-(N-methyl)leucine-dehydro-proline-lactate-glutamine-pyroglutamate,

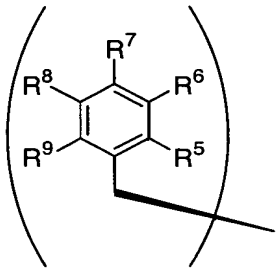
-(N-methyl)leucine-dehydro-proline-lactate-glutamine-cyclopentanoate,

-(N-methyl)leucine-dehydro-proline-alanine-leucine-pyroglutamate, and

-(N-methyl)leucine-dehydro-proline-(N-methyl-alanine)-leucine-pyroglutamate;

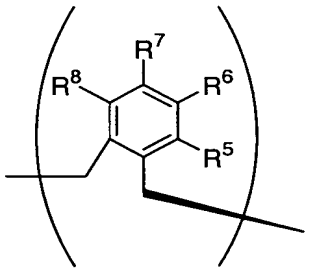
ii) ~~either~~ R^2 and R^3 are one of

(a) R^3 is selected from the group consisting of $-CH_3$ and -H; and R^2 is selected from the group consisting of an isoleucine side chain, a valine side chain, an alanine side chain, a norleucine side chain, a norvaline side chain, a leucine side chain, a histidine side chain, a tryptophan side chain, an arginine side chain, a lysine side chain, a second fluorophore, and a substituent having the structure



; ~~or~~ and

(b) R^2 and R^3 together are a substituent having the structure



;

iii) each of R^5, R^6, R^7, R^8, and R^9, when present, is independently selected from the group consisting of -H, -OH, $-OCH_3$, $-CO(C_6H_5)$, -Br, -I, -F, -Cl, $-CH_3$, and $-C_2H_5$;

iv) R^4 is selected from the group consisting of an isoleucine side chain and a valine side chain;

v) X is selected from the group consisting of -O- and ~~-(NH)-~~ -NH-;

vi) Y is selected from the group consisting of -H and a hydroxyl protecting group;

vii) R^{10} is selected from the group consisting of a leucine side chain and a lysine side chain; and

viii) the molecule is not tamandarin A.

28. (Original) The composition of claim 27, wherein R^1 is selected from the group consisting of

-(N-methyl)leucine-deoxo-(S)proline,

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate,

-(N-methyl)leucine-deoxo-(S)proline-pyruvate,

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-(a first fluorophore),

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-glutamine-pyroglutamate,

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-glutamine-cyclopentanoate,

-(N-methyl)leucine-deoxo-(S)proline-alanine-leucine-pyroglutamate,

-(N-methyl)leucine-deoxo-(S)proline-(N-methyl-alanine)-leucine-pyroglutamate,

-(N-methyl)leucine-dehydro-(S)proline,

-(N-methyl)leucine-dehydro-(S)proline-(S)lactate,

-(N-methyl)leucine-dehydro-(S)proline-pyruvate,

-(N-methyl)leucine-dehydro-(S)proline-(S)lactate-(a first fluorophore),

-(N-methyl)leucine-dehydro-(S)proline-(S)lactate-glutamine-pyroglutamate,

-(N-methyl)leucine-dehydro-(S)proline-(S)lactate-glutamine-cyclopentanoate,

-(N-methyl)leucine-dehydro-(S)proline-alanine-leucine-pyroglutamate and

-(N-methyl)leucine-dehydro-(S)proline-(N-methyl-alanine)-leucine-pyroglutamate.

29. (Currently Amended) The composition of claim 27, wherein R^1 is selected from the group consisting of

~~-(N-methyl)leucine-deoxo-(S)proline,~~

~~-(N-methyl)leucine-deoxo-(S)proline-(S)lactate,~~

~~-(N-methyl)leucine-deoxo-(S)proline-pyruvate,~~

~~-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-(a first fluorophore),~~

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-(S)glutamine-(S)pyroglutamate,

-(N-methyl)leucine-deoxo-(S)proline-(S)lactate-(S)glutamine-(S)cyclopentanoate,

-(N-methyl)leucine-deoxo-(S)proline-(S)alanine-(S)leucine-(S)pyroglutamate,

-(N-methyl)leucine-deoxo-(S)proline-(N-methyl-S-alanine)-(S)leucine-(S)pyroglutamate,

~~-(N-methyl)leucine-dehydro-(S)proline,~~

~~-(N-methyl)leucine-dehydro-(S)proline-(S)lactate,~~

~~-(N-methyl)leucine-dehydro-(S)proline-pyruvate,~~

~~-(N-methyl)leucine-dehydro-(S)proline-(S)lactate-(a first fluorophore),~~

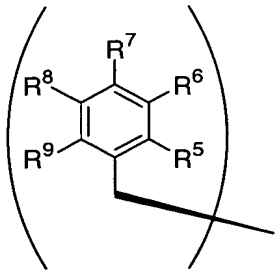
-(N-methyl)leucine-dehydro-(S)proline-(S)lactate-(S)glutamine-(S)pyroglutamate,

-(N-methyl)leucine-dehydro-(S)proline-(S)lactate-(S)glutamine-(S)cyclopentanoate,

-(N-methyl)leucine-dehydro-(S)proline-(S)alanine-(S)leucine-(S)pyroglutamate, and

-(N-methyl)leucine-dehydro-(S)proline-(N-methyl-S-alanine)-(S)leucine-(S)pyroglutamate.

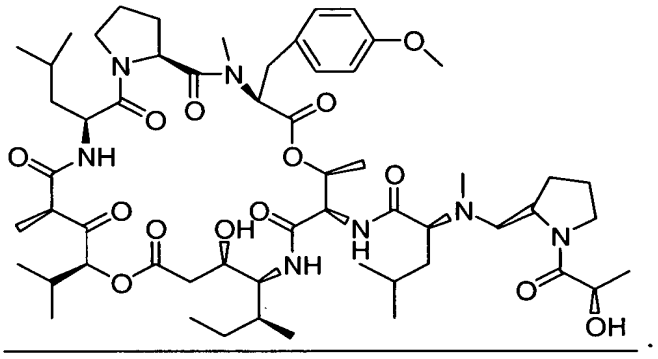
30. (Currently Amended) The composition of claim 27, wherein R^2 is



,

R^3 is methyl, R^4 is an isoleucine side chain, each of R^5, R^6, R^8, and R^9 is ~~a hydride radical~~ -H, R^7 is methoxy, R^{10} is a leucine side chain, X is -O-, and Y is ~~a hydride radical~~ -H.

31. (Currently Amended) The compound of claim 27, wherein the didemnin analog is compound 202 having the structure



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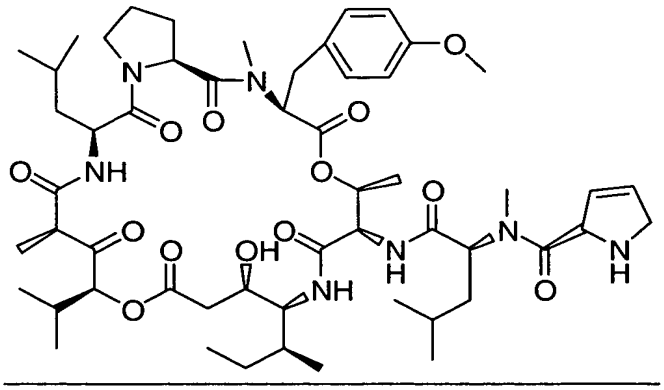
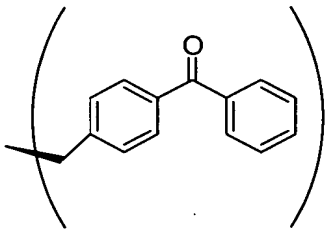
32. (Currently Amended) The composition of claim 27, wherein the didemnin analog is compound 204 having the structure



33. (Original) The composition of claim 27, wherein R^1 is -(N-methyl)leucine-deoxo-(S)proline-lactate.

34. (Currently Amended) The composition of claim 27, wherein Y is -H, and wherein R^2 has the structure



35. (Original) The composition of claim 27, wherein R^2 is a lysine side chain and Y is -H.

36. (Currently Amended) The composition of claim 27, wherein X is ~~-(NH)-~~ -NH-.

37. (Original) The composition of claim 27, further comprising a pharmaceutically acceptable carrier.

38. (Original) A support covalently attached with the didemnin analog of claim 27.

39. (Original) A method of inhibiting protein synthesis in a cell, the method comprising administering the composition of claim 27 to the cell.

40. (Original) A method of inhibiting growth of a cell, the method comprising administering the composition of claim 27 to the cell.

41. (Original) A method of inhibiting proliferation of a cell, the method comprising administering the composition of claim 27 to the cell.

42. (Original) A method of inhibiting tumorigenesis in a cell, the method comprising administering the composition of claim 27 to the cell.

43. (Original) A method of enhancing apoptosis of a cell, the method comprising administering the composition of claim 27 to the cell.

44. (Currently Amended) A method of ~~making~~ preparing a tamandarin or didemnin analog ~~the improvement~~ comprising incorporating a deoxo-proline residue in place of a proline residue of the analog in a chemical reaction to prepare said tamandarin or didemnin analog.

45. (Currently Amended) The ~~improvement~~ method of claim 44, wherein the analog comprises an (N-methyl)leucine-proline moiety and wherein the (N-methyl)leucine-proline moiety is replaced by an (N-methyl)leucine-deoxo-proline moiety.

46. (Currently Amended) The ~~improvement~~ method of claim 45 wherein the (N-methyl)leucine-deoxo-proline is made by

reducing the ester function of proline to an aldehyde function; and

coupling the proline with the (N-methyl)leucine moiety by reductive amination to yield the (N-methyl)leucine-deoxo-proline moiety.

47. (Currently Amended) The ~~improvement~~ method of claim 46, wherein the amine moiety of the proline is protected with an amine-protecting group prior to the reductive amination.

48. (Currently Amended) The ~~improvement~~ method of claim 46, wherein the ester function of the proline is reduced to an aldehyde function by contacting the proline with a strong base and then contacting the proline with an oxidizing agent.

49. (Currently Amended) The ~~improvement~~ method of claim 46, wherein the reductive amination is performed in a non-aqueous solvent in the presence of a strong base and a carboxylic acid catalyst.

50. (Currently Amended). ~~In a~~ A method of ~~making~~ preparing a tamandarin or didemnin analog the improvement comprising incorporating a dehydro-proline residue in place of a proline residue of the analog in a chemical reaction used to prepare said tamandarin or didemnin analog.

51. (Currently Amended) The ~~improvement~~ method of claim 50, wherein the analog comprises an (N-methyl)leucine-proline moiety and wherein the (N-methyl)leucine-proline moiety is replaced by an (N-methyl)leucine-dehydro-proline moiety.

52. (Currently Amended) The ~~improvement~~ method of claim 50, wherein the dehydro-proline residue is made by protecting the carboxyl and amino moieties of the 4-hydroxyprolinate, alkyl sulfonylating the 4-hydroxyl moiety, displacing the alkyl-sulfonate moiety with an aryl-selenyl moiety, oxidatively eliminating

the aryl-selenyl moiety to yield a dehydro-proline moiety having protected carboxyl and amine moieties, and coupling the dehydro-proline moiety with an amine moiety of the analog.

53. (Currently Amended) The ~~improvement~~ method of claim 50, wherein the alkyl-sulfonate moiety is a methyl-sulfonate moiety.

54. (Currently Amended) The ~~improvement~~ method of claim 50, wherein the aryl-selenyl moiety is a phenyl-selenyl moiety.

55. (Currently Amended) The ~~improvement~~ method of claim 50, wherein the 4-hydroxyprolinate is trans-4-hydroxyprolinate.

56. (New) The composition of claim 1, wherein the analog is substantially pure.

57. (New) The composition of claim 5, wherein the analog is substantially pure.

58. (New) The composition of claim 6, wherein the analog is substantially pure.

59. (New) The composition of claim 10, wherein the analog is substantially pure.

60. (New) The composition of claim 19, wherein the analog is substantially pure.

61. (New) The composition of claim 27, wherein the analog is substantially pure.